

## **REMARKS**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **I. DISPOSITION OF THE CLAIMS**

Claims 1-2, 4, 8-9, 24-26, 29-31 and 42 are currently being amended. No new matter has been added. The specification provides clear support, literally or as “clearly conveyed”.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-4, 8-9, 24-26, 29-31, and 42 are now pending in this application.

### **II. OBJECTIONS BASED ON DRAWINGS**

Figure 1 stands objected to for failure to depict PV. Office Action, page 2, lines 8-10. Applicants traverse. Applicants submit that a person of ordinary skill in the art would readily understand how Figure 1 explains the role of JAK2 in PV, to the extent necessary for the purposes of patentability. The Office has not provided any legal basis to require more.

Figure 9 stands objected to for omitting labels or explanation for depicted lanes. Office Action, page 2, lines 11-12. Applicants traverse. The specification explains that the lanes represent human erythroleukaemia (HEL) cells, including an untreated control (0) and six treated HEL cells, and the specification also explains the lanes designated as C+ and C- (see pages 9-10, paragraphs [0129] – [0132] of publication US 2006-0288432):

[0129] **FIGS. 8 and 9:** Expression of V617F Jak2 in HEL cells is reduced 24 hours after treatment with siRNA specific to JAK2 V617F Jak2(siRNA #1, 3 and 4).

[0130] 0 to 6: HEL cells treated (1 to 6) or non-treated (0) with siRNA V617F Jak2.

[0131] C+: 293HEK cells transfected with the V617F Jak2RV vector

[0132] C-: 293 HEK

No further explanation of Figure 9 would appear to be necessary.

The Office objects to the specification, specifically the legends to Figures 2, 3, 5, and 9-10 for allegedly not clearly explaining the data of the figures and also for lack of explanation of two depicted panels in Figure 5. Office Action, page 2, lines 14-16.

A person of ordinary skill in the art would understand the data of Figures 2, 3, 5, and 9-10 to the extent necessary to understand the invention as claimed. Further explanation or revision of these figures is unnecessary to satisfy any aspect of the requirement of § 112 relating to sufficiency of disclosure.

Accordingly, Applicants request withdrawal of the objections based on the figures.

### **III. SECTION 101 REJECTION**

The Office rejected claim 4 under 35 U.S.C. § 101 as non-statutory because the subject matter thereof allegedly “are likely to occur in nature”. The Office suggested amending the claims to recite “isolated” or “recombinant”. Office Action, page 4, lines 12-14.

Applicants traverse this rejection as unfounded.

To further prosecution, however, this rejection has been obviated by amendment. Claim 4 has been amended to recite “recombinant mammalian cell” as suggested by the Office. Accordingly, Applicants request withdrawal of this ground of rejection.

### **IV. INDEFINITENESS REJECTIONS**

The claims stand rejected as indefinite under 35 U.S.C. § 112, second paragraph, for various grounds. Applicants request that the Office withdraw this ground of rejection in view of the amendments and arguments below.

#### **A. Claim 1**

Claim 1 stands rejected as indefinite due the limitations identifying the JAK2 mutation.

Applicants traverse this rejection as unfounded.

To further prosecution, however, claim 1 has been amended as suggested by the Office to recite an “isolated variant of human JAK2 ~~protein~~ (Janus kinase 2) protein, wherein

the variant has a ~~comprising the~~ V617F mutation and ~~having~~ has the sequence shown in SEQ ID NO: 1”.

**B. Claim 8-9 and 24-26**

Claims 8-9 and 24-26 stand rejected as indefinite for the limitations “position 1849”, “G1849T”, and “t<sup>1849</sup>”.

Applicants have obviated this ground of rejection by amending claim 8 to refer to the specific positions of the JAK2 mutation in each of SEQ ID NO 3 (t<sup>261</sup>) and SEQ ID NO 4 (t<sup>50</sup>). Claims 9 and 24-26 depend directly or indirectly from claim 8 and are included in this rejection for that reason alone. Thus, the rejection is also obviated for claims 9 and 24-26.

The specification defines “V617F mutation”, “variant JAK2 V617F”, “G1849T”, and by inference “t<sup>1849</sup>” in a manner that would be abundantly clear to a person of ordinary skill in the art. The specification discloses the specific position of the JAK2 mutation in SEQ ID NO 3 on page 4, paragraph [0030] of publication US 2006-0288432, where the mutation is explicitly designated as “t<sup>1849</sup>”. The identical mutation appears in position 261 in SEQ ID NO 3 and in position 50 in SEQ ID NO 4.

The specification precisely defines the 1849 position of mutation “t<sup>1849</sup>” by reference to SEQ ID NO 2 as follows (see page 2 of publication US 2006-0288432):

[0014] Therefore, according to a first characteristic, the present invention concerns the isolated protein JAK 2 (Janus kinase 2), in particular the Homo sapiens Janus kinase 2 protein (NCBI, accession number NM\_004972; G1:13325062) comprising a mutation on amino acid 617 (codon 617 of the cDNA starting from ATG) more particularly the V617F mutation, hereinafter called variant JAK2 V617F such as presented in SEQ ID N°1 below:

[0016] The invention also relates to a nucleotide sequence encoding SEQ ID N°1, preferably SEQ ID N°2 (sequence of the human JAK2 gene with the TTC codon instead of GTC on codon 617 (g/t mutation at position 1849 hereinafter called G1849T, starting from the ATG marking the start of translation).

The reference starting point ATG appears in SEQ ID NO 1 at position 495. The relevant mutation appears at position 2343 (i.e., at position 1849 treating position 495 as the starting point). The specification discloses the corresponding mutation “V617F” explicitly

within SEQ ID NO 1 as “F<sup>617</sup>”. See publication US 2006-0288432, page 2, paragraph [0014]. SEQ ID NO 1 shows at position 617 the corresponding amino acid “Phe” resulting from the mutation. See publication US 2006-0288432, page 16.

The Office also asserted regarding claims 24-26 and 29, “Any claim reciting an amino acid or nucleotide residue must also recite a sequence identifier number (SEQ ID NO: ) in order to comply with 35 U.S.C. 112, second paragraph”. Office Action, page 5, lines 5-7.

Applicants respectfully traverse. Claims 24-26 and 29 already satisfy the stated requirement, because each claim depends from a base claim that recites a SEQ ID NO. Claims 24-26 are kit claims that refer to “probes or primers such as defined in claim 8” where claim 8 recites “SEQ ID NO 3 or 4”. To further obviate this rejection Applicants have amended the preamble of claim 29 to match the amendment to claim 1; thus, claim 29 now recites “expression of the ~~JAK2-V617F~~ isolated variant of human JAK2 protein according to claim 1”.

In sum, the limitations “position 1849”, “G1849T”, and “t<sup>1849</sup>” would be clearly understood by a person of ordinary skill in the art, and this rejection should be withdrawn.

**C. “Improper antecedent usage”**

Claims 1-4, 8, 9, 24-26, 29-31, and 42 stand rejected for “improper antecedent usage”. Office Action, page 5, line 8 et seq.

Applicants have obviated this rejection by amendment.

**V. REJECTIONS UNDER SECTION 112, FIRST PARAGRAPH**

The claims stand rejected under 35 U.S.C. § 112, first paragraph on two grounds. Applicants traverse each ground as explained below.

**A. Enablement**

Claims 1-4, 8-9, 24-26, 28-31, and 42 stand rejected under 35 U.S.C. § 112, first paragraph, as non-enabled. The Office grounded the rejection on the “comprising” language of claim 1. Office Action, page 6, line 14, and page 8, penultimate line).

Applicants traverse this rejection as legally deficient.

To further prosecution, however, Applicants have obviated this ground of rejection by amending claim 1 to recite “An isolated variant of human JAK2 ~~protein~~ (Janus kinase 2)

protein, wherein the variant has a ~~comprising the~~ V617F mutation, and ~~has~~ having the sequence shown in SEQ ID NO 1.” Claims 2-4, 29-31, and 42 depend directly or indirectly from claim 1 (claim 28 was canceled). As such, the amendment to claim 1 also obviated this ground of rejection for claims 2-4, 29-31, and 42.

Regarding claim 8, Applicants have amended claim 8 to specifically recite the positions of the mutation in the referenced SEQ ID NOs. Applicants submit that claim 8 as amended is fully enabled by the specification. The same reasoning applies to claims 9 and 24-26, which depend directly or indirectly from claim 8.

Accordingly, Applicants request withdrawal of this ground of rejection.

**B. Possession**

Claims 1-4, 24-26, and 29-31 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description/possession. Office Action, pages 10-12.

The Office rejected claims 1, 4, and 42 due to the scope of proteins. Office Action, page 10, lines 7-10.

Applicants traverse this rejection as legally deficient.

To further prosecution, however, Applicants have obviated this ground of rejection by amendment, as noted above in addressing enablement. Thus, the claims fully satisfy the written description/possession requirement of § 112, first paragraph.

Accordingly, Applicants request withdrawal of this ground of rejection.

**CONCLUSION**

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect

information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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